



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Manuel Vega et al.  
Serial No. : 10/022,249  
Filed : December 17, 2001  
Cust. No. : 77202  
Title : HIGH THROUGHPUT DIRECTED EVOLUTION BY RATIONAL  
MUTAGENESIS

Art Unit : 1631  
Examiner : Jerry Lin  
Conf. No. : 7196

**Mail Stop Amendment**  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IN  
ACCORDANCE WITH 37 C.F.R. §§1.97-1.98**

Dear Sir:


Because this Supplemental Information Disclosure Statement is filed after the receipt of a First Office Action on the Merits for the above-captioned application, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 02-1818.

In accordance with the duty of disclosure imposed by 37 C.F.R. §1.56 to inform the Patent Office of all information known by Applicant or Applicant's representative that may be material to the examination of the subject application, Applicant's representative hereby provides this Supplemental Information Disclosure Statement that is prepared in accordance with 37 C.F.R. §§1.97-1.98. Form PTO-1449 (1 page) and copies of the cited non U.S. patent documents are provided herewith in connection with the above-captioned application.

The documents listed on the Form PTO-1449 are in the English language. Hence, in accordance with the requirements of 37 C.F.R. §1.98, as amended effective March 16, 1992, no further explanation of the listed items is necessary.

A copy of a Communication from the European Patent Office (Document I), issued April 14, 2008, in connection with corresponding European Patent Application No. 02798018.4 regarding the intention to grant an European patent is provided. A copy of an Office Action,

CERTIFICATE OF MAILING BY "EXPRESS MAIL"  
"Express Mail" Mailing Label Number EM 315453677 US  
Date of Deposit April 16, 2009.  
I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA, 22313-1450.

  
Christopher Ochs

Applicant : Manuel Vega et al.  
Serial No. : 10/022,249  
Filed : December 17, 2001

(Document II), issued September 16, 2008, in connection with co-owned U.S. Application Ser. No. 10/658,355 is provided. A Copy of an Office Action, (Document III), issued December 24, 2008, in connection with co-owned U.S. Application Ser. No. 11/707,014 is provided. The table below lists Documents I-III and includes a column that provides a space next to the documents to be considered, for the Examiner's initials.

Examiner Initial	Document No.	Document
	I	Copy of Communication from European Patent Office, issued April 14, 2008, in connection with corresponding European Patent Application No. 02798018.4
	II	Copy of Office Action, issued September 16, 2008, in connection with U.S. Application Ser. No. 10/658,355
	III	Copy of Office Action, issued December 24, 2008, in connection with U.S. Application Ser. No. 11/707,014

In the Office Actions, dated May 13, 2008 and October 16, 2008, the Examiner indicated that the Information Disclosure Statements (IDSs) submitted on February 7, 2008 and July 10, 2008, were considered and initialed by the Examiner. The IDS filed on February 7, 2008 contained a Table listing Office Actions and European Examination Reports cited in related and corresponding U.S. and foreign Patent Applications. The IDS filed on July 10, 2008 contained a Table listing an International Search Report cited in a related foreign Patent Application. These tables were not initialed by the Examiner. These IDSs included the application number of the application in which the IDS was being submitted, a column that provides a blank space next to each citation for the Examiner's initials, a heading on the listing that clearly indicates the list is an Information Disclosure Statement, and copies of listed documents. Therefore, the February 7, 2008 and July 10, 2008 IDSs are in compliance with 37 CFR §§ 1.97, 1.98 and MPEP § 609 and Applicant respectfully requests that Examiner consider and initial all information listed in the tables submitted in the IDSs filed February 7, 2008 and July 10, 2008.

Further to the list provided in the communication filed on July 10, 2008, applicant also makes known to the examiner the following pending U.S. and International Applications that have one or more common inventors and/or are common ownership:

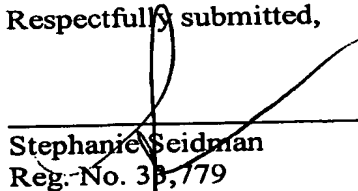
Applicant : Manuel Vega et al.  
Serial No. : 10/022,249  
Filed : December 17, 2001

U.S.S.N.	Filing Date	Publ. No.	Publ. Date	Docket No.
11/704,141	02/07/07	2008-0194477	08/14/08	922D
11/706,088	02/13/07	2008-0274081	11/06/08	922F
11/788,836	04/19/07	2008-0260820	10/23/08	932
12/082,365	04/09/08	2008-0274081	11/06/08	922I
12/082,389	04/09/08	2009-0053147	02/26/09	922J
Int'l App. No.	Filing Date	Publ No.	Publ. Date	Docket No.
PCT/GB07/004520	11/27/2007	WO 08/065372	06/05/08	931PC

Although these documents and applications are made known to the Patent and Trademark Office in compliance with Applicant's duty of disclosure, such disclosure is not to be construed as an admission by Applicant or Applicant's representative that any of the information, singly or in any combination thereof, is effective as prior art against the subject application. In accordance with 37 C.F.R. §1.97 (g and h), the filing of this Supplemental Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 C.F.R. §1.56 (b) exists.

Applicant respectfully requests that the Examiner review the foregoing documents and make them of record in the file history of the above-captioned application.

Respectfully submitted,

  
Stephanie Seidman  
Reg. No. 38,779

Attorney Docket No. 0119365-00002 / 911  
Address all correspondence to:  
Stephanie Seidman  
K&L Gates LLP  
3580 Carmel Mountain Road, Suite 200  
San Diego, California 92130  
Telephone: (858) 509-7410  
Facsimile: (858) 509-7460  
email: stephanie.seidman@klgates.com

**Attachment 2: Copy of Information Disclosure Statement,  
filed July 10, 2008, in U.S. Application Serial No.  
10/022,249**



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Manuel Vega et al.  
Serial No. : 10/022,249  
Filed : December 17, 2001  
Cust. No. : 77202  
Title : HIGH THROUGHPUT DIRECTED EVOLUTION BY RATIONAL  
MUTAGENESIS

Art Unit : 1631  
Examiner : Jerry Lin  
Conf. No. : 7196

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IN  
ACCORDANCE WITH 37 C.F.R. §§1.97-1.98**

Dear Sir:

This Supplemental Information Disclosure Statement is filed after a Request for Continued Examination of the above-captioned application and prior to receipt of an Office Action. Thus, a fee for filing this statement should not be due. If, however, it is determined that a fee is due, any fees that may be due in connection with filing this paper may be charged to Deposit Account No. 02-1818.

In accordance with the duty of disclosure imposed by 37 C.F.R. §1.56 to inform the Patent Office of all information known by Applicant or Applicant's representative that may be material to the examination of the subject application, Applicant's representative hereby provides this Supplemental Information Disclosure Statement that is prepared in accordance with 37 C.F.R. §§1.97-1.98. Form PTO-1449 (1 page) and copies of the cited non U.S. patent documents are provided herewith in connection with the above-captioned application.

The documents listed on the Form PTO-1449 are in the English language. Hence, in accordance with the requirements of 37 C.F.R. §1.98, as amended effective March 16, 1992, no further explanation of the listed items is necessary.

CERTIFICATE OF MAILING BY "EXPRESS MAIL"  
"Express Mail" Mailing Label Number EM 247737964 US  
Date of Deposit July 10, 2008  
I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA, 22313-1450.

  
Steven Dennis

Applicant : Manuel Vega et al.  
Serial No. : 10/022,249  
Filed : December 17, 2001

A Copy of an International Search Report, (Document I), issued June 13, 2008, in connection with co-owned International Application No. PCT/US2007/014219 is provided. The table below lists Documents I and includes a column that provides a space next to the documents to be considered, for the Examiner's initials.

Examiner Initial	Document No.	Document
	I	Copy of International Search Report, issued June 13, 2008, in connection with co-owned International Application No. PCT/US2007/014219

In the International Search Report, (Document I), issued June 13, 2008, the following document is cited: Chang et al., "Identification of functionally important residues of the epidermal growth factor-2 domain of factor IX by alanine-scanning mutagenesis. Residues Asn(89)-Gly(93) are critical for binding factor VIIIa." *J Biol Chem* 277:25393-25399 (2002). Document 1 is made of record in the instant application in this Information Disclosure Statement, supplied with Forms PTO-1449 and copies of the cited non U.S. patent documents.

In the Office Action dated May 13, 2008, the Examiner indicated that the Information Disclosure Statement (IDS) submitted on February 7, 2008 was considered and initialed by the Examiner. The IDS filed on February 7, 2008 contained a Table listing Office Actions and European Examination Reports cited in related and corresponding U.S. and foreign Patent Applications. This Table was not initialed by the Examiner. The Information Disclosure Statement includes the serial number of the application for which the IDS was submitted, a heading that clearly indicates the list is an Information Disclosure Statement, a Table containing a column with a blank space next to each citation for the Examiner's initials and copies of cited documents. Therefore, the February 7, 2008 IDS is in compliance with 37 CFR §§ 1.97, 1.98 and MPEP § 609. Applicant respectfully requests that the Examiner consider and initial all information listed in the Table submitted in the IDS filed February 7, 2008.

Further to the list provided in the Information Disclosure Statement filed on February 7, 2008, Applicant also makes known to the Examiner the following pending U.S. and International Applications that have one or more common inventors and/ or are commonly owned:

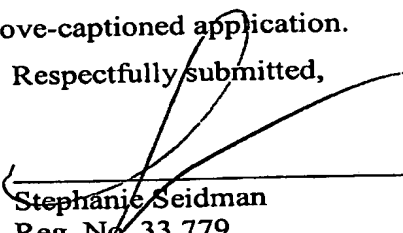
Applicant : Manuel Vega et al.  
Serial No. : 10/022,249  
Filed : December 17, 2001

U.S.S.N.	Filing Date	Publ. No.	Publ. Date	Docket No.
11/703,610	02/06/07	2008-0075672	03/27/08	922C
11/729,267	03/27/07	2008-0038224	02/14/08	924
11/729,266	03/27/07	2008-0003202	01/03/08	924B
11/818,985	06/15/07	2008-0102115	05/01/08	930
11/825,604	07/05/07	2008-0159977	07/03/08	922H
11/998,387	11/28/07	n/a	n/a	931
12/082,365	04/09/08	n/a	n/a	922I
12/082,389	04/09/08	n/a	n/a	922J
12/157,150	06/06/08	n/a	n/a	922K
Int'l App. No.	Filing Date	Publ No.	Publ. Date	Docket No.
PCT/GB07/004520	11/27/2007	n/a	n/a	931PC

Although these documents and applications are made known to the Patent and Trademark Office in compliance with Applicant's duty of disclosure, such disclosure is not to be construed as an admission by Applicant or Applicant's representative that any of the information, singly or in any combination thereof, is effective as prior art against the subject application. In accordance with 37 C.F.R. §1.97 (g and h), the filing of this Supplemental Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 C.F.R. §1.56 (b) exists.

Applicant respectfully requests that the Examiner review the foregoing documents and make them of record in the file history of the above-captioned application.

Respectfully submitted,

  
Stephanie Seidman  
Reg. No. 33,779

Attorney Docket No. 119365-00002 / 911  
Address all correspondence to:  
Stephanie Seidman  
Bell, Boyd & Lloyd LLP  
3580 Carmel Mountain Road, Suite 200  
San Diego, California 92130  
Telephone: (858) 509-7410  
Facsimile: (858) 509-7460  
email: sseidman@bellboyd.com

**Attachment 3: Copy of Information Disclosure Statement,  
filed February 7, 2008, in U.S. Application Serial No.  
10/022,249**





Attorney's Docket No.: 17109-002001 / 911

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Manuel Vega et al.  
Serial No. : 10/022,249  
Filed : December 17, 2001  
Cust. No. : 20985  
Title : HIGH THROUGHPUT DIRECTED EVOLUTION BY RATIONAL  
MUTAGENESIS

Art Unit : 1631  
Examiner : Jerry Lin  
Conf. No. : 7196

**Mail Stop Amendment**  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT IN  
ACCORDANCE WITH 37 C.F.R. §§1.97-1.98**

Dear Sir:

Because this Supplemental Information Disclosure Statement is after receipt of a first Office Action on the Merits of the above-captioned application, the filing fee of \$180 is enclosed. If no proper payment is enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 06-1050.

In accordance with the duty of disclosure imposed by 37 C.F.R. §1.56 to inform the Patent Office of all information known by Applicant or Applicant's representative that may be material to the examination of the subject application, Applicant's representative hereby provides this Supplemental Information Disclosure Statement that is prepared in accordance with 37 C.F.R. §§1.97-1.98. Form PTO-1449 (1 page) and copies of the cited non U.S. patent documents are provided herewith in connection with the above-captioned application.

CERTIFICATE OF MAILING BY "EXPRESS MAIL"  
"Express Mail" Mailing Label Number EV 965985825 US  
Date of Deposit February 7, 2008  
I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA, 22313-1450.

02/12/2008 CCHAU1 00000070 10022249

01 FC:1806

180.00 DP

Stephanie Seidman

Applicant : Manuel Vega et al.  
Serial No. : 10/022,249  
Filed : December 17, 2001

Attorney's Docket No.: 17109-002001 / 911  
Supplemental Information Disclosure Statement

The documents listed on the Form PTO-1449 are in the English language. Hence, in accordance with the requirements of 37 C.F.R. §1.98, as amended effective March 16, 1992, no further explanation of the listed item is necessary.

A copy of a European Examination Report (Document I), issued July 31, 2007, in connection with corresponding European Patent Application No. 02798018.4 is provided. Copies of three U.S. Office Actions (Documents II, III and IV), issued May 9, 2006, March 12, 2007, and December 10, 2007, respectively, in connection with co-owned U.S. Application Ser. No. 10/658,355 are provided. Copies of two European Examination Reports (Documents V and VI), issued August 2, 2005 and June 2, 2006, respectively, in connection with European Patent Application No. 03748392.2 are provided. European Patent Application No. 03748392.2 corresponds to U.S. Application Ser. No. 10/658,355. The table below lists Documents I-VI and includes a column that provides a space next to the documents to be considered, for the Examiner's initials.

Examiner Initial	Document No.	Document
	I	Copy of European Examination Report, issued July 31, 2007, in connection with European Patent Application No. 02798018.4
	II	Copy of U.S. Office Action, issued May 9, 2006, in connection with U.S. Application Ser. No. 10/658,355
	III	Copy of U.S. Office Action, issued March 12, 2007, in connection with U.S. Application Ser. No. 10/658,355
	IV	Copy of U.S. Office Action, issued December 10, 2007, in connection with U.S. Application Ser. No. 10/658,355
	V	Copy of European Examination Report, issued August 2, 2005, in connection with European Patent Application No. 03748392.2
	VI	Copy of European Examination Report, issued June 2, 2006, in connection with European Patent Application No. 03748392.2

In the U.S. Office Action, issued May 9, 2006 (Document II), three documents are cited: 1) US 5,096,815, 2) Alam et al., "Expression and purification of a mutant human growth hormone that is resistant to proteolytic cleavage by thrombin, plasmin and human plasma in vitro," *J. Biochem.* 65:183-190 (1998), and 3) Chiang et al., "In vivo genetic analysis of bacterial virulence," *Ann. Rev. Microbiology* 53:129-154 (1999). Documents 1-3 are made of record in

Applicant : Manuel Vega et al.  
Serial No. : 10/022,249  
Filed : December 17, 2001

Attorney's Docket No.: 17109-002001 / 911  
Supplemental Information Disclosure Statement

the instant application in an Information Disclosure Statement, supplied with Forms PTO-1449 and copies of the cited non U.S. patent documents, filed June 22, 2006. In the U.S. Office Action, issued March 12, 2007 (Document III), one document is cited: 1) Stabach et al., "Site-directed mutagenesis of alpha II spectrin at codon 1175 modulates its mu-calpain susceptibility," *Biochemistry* 36:57-65 (1997). Document 1 is made of record in the instant application in this Information Disclosure Statement, supplied with Forms PTO-1449 and copies of the cited non U.S. patent documents. In the U.S. Office Action, issued December 10, 2007 (Document IV), four documents are cited: 1) US 6,548,640, 2) Jones et al., "The rapid generation of mutation data matrices from protein sequences" *CABIOS* 8:275-282 (1992), 3) Alam et al., "Expression and purification of a mutant human growth hormone that is resistant to proteolytic cleavage by thrombin, plasmin and human plasma in vitro," *J. Biochem.* 65:183-190 (1998), and 4) Chiang et al., "In vivo genetic analysis of bacterial virulence," *Ann. Rev. Microbiology* 53:129-154 (1999). Documents 1-2 are made of record in the instant application in this Information Disclosure Statement, supplied with Forms PTO-1449 and copies of the cited non U.S. patent documents. Documents 3-4 are made of record in the instant application in an Information Disclosure Statement, supplied with Forms PTO-1449 and copies of the cited non U.S. patent documents, filed June 22, 2006.

In the European Examination Report, issued August 2, 2005 (Document V), five documents are cited: 1) US 5,223,409, 2) WO 01/61344, 3) Manetti et al., "Design and realization of a tailor-made enzyme to modify the molecular recognition of 2-arylpropionic esters by *Candida rugosa* lipase," *Biochem. Biophys. Acta.* 1543(1):146-158 (2000), 4) WO 03/023032 5) Lewerenz et al., "Shared receptor components but distinct complexes for alpha and beta interferons," *J. Mol. Biol.* 282(3):585-599 (1998). Documents 1-5 are made of record in the instant application in an Information Disclosure Statement, supplied with Forms PTO-1449 and copies of the cited non U.S. patent documents, filed March 15, 2005. In the European Examination Report, issued June 2, 2006 (Document VI), three documents are cited: 1) US 6,013,478, 2) WO 95/23813, 3) WO 01/32844. Documents 1-3 are made of record in the instant application in an Information Disclosure Statement, supplied with Forms PTO-1449 and copies of the cited non U.S. patent documents, filed March 15, 2005.

Applicant : Manuel Vega et al.  
Serial No. : 10/022,249  
Filed : December 17, 2001

Attorney's Docket No.: 17109-002001 / 911  
Supplemental Information Disclosure Statement

Further to the list provided in the communication filed on March 2, 2007, applicant also makes known to the examiner the following pending U.S. and International Applications that have one or more common inventors and/ or are commonly owned:

U.S.S.N.	Filing Date	Publication or Issue No.	Publication or Issue Date	Docket No.
11/267,871	11/03/05	2007-0249532	10/25/07	925
11/656,921	01/22/07	2007-0254838	11/01/07	922E
11/703,610	02/06/07	n/a	n/a	922C
11/704,141	02/07/07	n/a	n/a	922D
11/706,088	02/13/07	2007-0172459	07/26/07	922F
11/707,014	02/14/07	2007-0224665	09/27/07	922G
11/729,267	03/27/07	n/a	n/a	924
11/729,266	03/27/07	n/a	n/a	924B
11/788,836	04/19/07	n/a	n/a	932
11/818,985	06/15/07	n/a	n/a	930
11/825,604	07/05/07	n/a	n/a	922H
Int'l App. No.	Filing Date	Publication No.	Publication Date	Docket No.
PCT/IB06/002034	05/04/06	WO 06/120580	11/16/06	926PC
PCT/EP07/002700	03/27/07	WO 07/110231	10/04/07	924PC
PCT/US07/14219	06/15/07	n/a	n/a	930PC

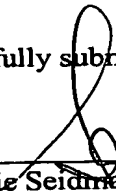
Although these documents and applications are made known to the Patent and Trademark Office in compliance with Applicant's duty of disclosure, such disclosure is not to be construed as an admission by Applicant or Applicant's representative that any of the information, singly or in any combination thereof, is effective as prior art against the subject application. In accordance with 37 C.F.R. §1.97 (g and h), the filing of this Supplemental Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 C.F.R. §1.56 (b) exists.

Applicant respectfully requests that the Examiner review the foregoing documents and make them of record in the file history of the above-captioned application.

Applicant : Manuel Vega et al.  
Serial No. : 10/022,249  
Filed : December 17, 2001

Attorney's Docket No.: 17109-002001 / 911  
Supplemental Information Disclosure Statement

Respectfully submitted,



---

Stephanie Seidman  
Reg. No. 33,779

Attorney Docket No. 17109-002001 / 911  
**Address all correspondence to:**  
Stephanie Seidman  
Fish & Richardson P.C.  
12390 El Camino Real  
San Diego, California 92130  
Telephone: (858) 678-4777  
Facsimile: (202) 626-7796  
email: seidman@fr.com